

**Remarks:**

This is in response to the Final Official Action of December 16, 2004 for the above-captioned application. Claims 1, 5, 6, 8 and 15 have been amended as is further discussed below. Claims 4 and 7 have been cancelled. New Claim 44 has been added as is further discussed below.

Claims 1, 2, 4-16, 25 and 26 have been rejected under 35 USC 102 as being allegedly anticipated by Pervarello et al. and Seki et al.

Purely for the sake of expediting prosecution, Applicants have amended Claim 1 to incorporate the limitations of now cancelled Claims 4 and 7. As amended, Claim 1 recites that  $R^1$  is  $(C_3-C_8)$ cycloalkyl or  $(C_5-C_{11})$ bicycloalkyl, wherein  $R^1$  is substituted with  $-NR^7C(=O)R^8$ ,  $(C_6-C_{14})$ aryl, (3-8 membered) heterocycloalkyl, or (5-14 membered) heteroaryl, which are each optionally substituted as recited in Claim 1. Claim 1 (and all claims dependent thereon directly or indirectly) as amended is not anticipated by Pervarello et al. or by Seki et al. In particular, Seki et al. recites a t-butyl group in the position corresponding to  $R_1$ . Pervarello et al. recites a cycloalkyl that may be substituted by a  $C_1-C_6$  alkyl group in the position corresponding to  $R_1$ . Accordingly, neither Pervarello et al. nor Seki et al. discloses the invention claimed in Claim 1 as amended. Claim 1 has also been amended to recite  $n=0$ , since, in view of the foregoing amendment, the claim is patentable over Pervarello et al. and Seki et al. for  $n = 0-3$ .

In view of the foregoing amendments and remarks, withdrawal of the rejection of Claims 1, 2, 4-16, 25 and 26 under 35 USC 102 as being allegedly anticipated by Pervarello et al. and Seki et al. is respectfully requested.

Claims 1, 2, 4-16, 25 and 26 have been rejected under 35 USC 103(a) as allegedly obvious over the combined teachings of Pervarello et al., Ferruccio et al., Malle et al., Lepage et al., Daidone et al. I-III, Sato, Burow, and Seki et al. The Official Action alleges that the cited references teach compounds generically embrace the instantly claimed compounds, and further that the references teach compounds that differ from the compounds disclosed herein as being homologs.

However, it is respectfully submitted that Claims 1, 2, 4-16, 25 and 26 are patentable over the cited art. As a preliminary matter, the Official Action cannot allege obviousness simply by taking several random references and combining them in the absence of a motivation or suggestion to do so. Indeed, the Official Action has failed to establish a prima facie case of obviousness, which requires, as a first step (MPEP 2142), "some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary

skill in the art, to modify the reference or to combine reference teachings.” The Official Action alleges that the motivation to make the instantly claimed comes from the alleged fact that the cited art discloses cyclic homologs of the instantly claimed structures, and cites In re Shetty, In re Wilder and ex parte Ruddy. However, all the cited cases refer to linear homologs, and a similar argument is not applicable to cyclic homologs. In fact, it is well-known in the art that cyclic systems of different sizes have markedly different properties, so that it would not be obvious to one skilled in the art replace, for example, a cyclopropyl group (such as is present in the compounds disclosed in Pervarello et al.) with a higher cycloalkyl group.

Moreover, as discussed hereinabove, the compounds claimed in Claim 1 as amended differ with regard to the substitution of the cycloalkyl or bicycloalkyl group R<sub>1</sub>. Accordingly, the cases cited by the Official Action are irrelevant to the patentability of Claim 1. There is no disclosure or suggestion in the cited references, alone or in combination, to make compounds wherein R<sup>1</sup> is (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl or (C<sub>5</sub>-C<sub>11</sub>)bicycloalkyl wherein R<sup>1</sup> is substituted with -NR<sup>7</sup>C(=O)R<sup>8</sup>, (C<sub>6</sub>-C<sub>14</sub>)aryl, (3-8 membered) heterocycloalkyl, or (5-14 membered) heteroaryl, as expressly recited in Claim 1 as amended. Accordingly, the invention claimed in Claim 1 (and all claims dependent thereon) would not be obvious.

In view of the foregoing amendments and remarks, withdrawal of the rejection of Claims 1, 2, 4-16, 25 and 26 under 35 USC 103(a) as allegedly obvious over the combined teachings of Pervarello et al., Ferruccio et al., Malle et al., Lepage et al., Daidone et al. I-III, Sato, Burow, and Seki et al is respectfully requested.

The Official Action next refers to a rejection under 35 USC 112, first paragraph, for alleged lack of enablement of the recitation of Alzheimer's disease. Although the rejected claims are not identified, Applicants assume that the rejected claim is Claim 26, which recites Alzheimer's disease as a condition that may be treated. The Official Action alleges that “the disclosure provides no indication of whether the compounds treat any Alzheimer's disease,” and cites *Genentech, Inc. v. Novo Nordisk A/S (CAFC)* 42 USPQ 2d. 1001 in support of its conclusion of alleged non- enablement.

However, it is respectfully submitted that Claim 26 is enabled by the specification. As is clearly described in the specification, there is a known relationship between CDK5 inhibition and the treatment of Alzheimer's disease. *See, e.g., J. Biochem*, 117, 741-749 (1995), which discloses that cdk5 is involved in the phosphorylation of tau protein, which is in turn related to neurodegenerative disorders. The Official Action's statement that one of skill in the art would

need to determine which compound “actually treats” Alzheimer’s disease (page 8, first sentence) is based on an incorrect premise, since it is settled law that it is not required for patentability to show that a compound “actually treats” a condition recited in the claims. *See, e.g., In re Isaacs*, 347 F.2d 889 (CCPA 1963) and *In re Lanfer* (503 F.2d 1380), both of which stand for the proposition that it is not necessary to provide evidence from human clinical trials. Accordingly, the correct inquiry is not whether a compound “actually treats” a condition recited in the claims, but rather whether there is any relevant evidence in this regard. *See, e.g., In re Citron*, 325 F.2d 248 (CCPA 1963). In this case, the J. Biochem, 117, 741-749 (1995) article cited hereinabove is a clearly relevant evidence that CDK5 inhibition is related to the treatment of Alzheimer’s disease.

In view of the foregoing remarks, Applicants submit that the treatment of Alzheimer’s disease with the compounds of Formula I is clearly enabled. Accordingly, withdrawal of the rejection of Claim 26 under 35 USC 112, first paragraph, for alleged lack of enablement of the recitation of Alzheimer’s disease is respectfully requested.

Claims 1, 7 and 16 have been rejected as allegedly indefinite under 35 USC 112, second paragraph. The Official Action alleges that certain recitations in Claim 7 lack antecedent basis, and that Claim 16 does not recite affirmatively process/method steps. Claim 16 has also been rejected under 35 USC 101.

With regard to Claim 7, it is respectfully submitted that the rejection is now moot, since – as discussed hereinabove – the limitations in question have been incorporated in Claim 1 as amended.

With regard to Claim 16, Applicants submit that the rejections under either 35 USC 112 or under 35 USC 101 are unfounded. Claim 16 is directed to a pharmaceutical composition, not a process or method, and is therefore not required to recite affirmatively any process/method steps. It is possible that the Official Action contains a typographical error, and that Claim 26 (and not 16) was intended. However, Claim 26 depends on Claim 25, which *does* recite “comprising administering to the mammal a compound of claim 1 in an amount effective in treating said disease or condition”, an affirmative step. Accordingly, Claim 26 is not indefinite, and fully satisfies the requirements of both 35 USC 112 and 35 USC 101.

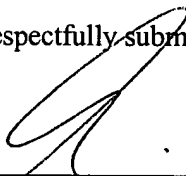
In view of the foregoing amendments and remarks, withdrawal of the rejection of Claims 1, 7 and 16 (or 26) under 35 USC 112, second paragraph and/or under 35 USC 101 is respectfully requested.

New Claim 44 has been added to further claim the invention. New Claim 44 claims a compound of claim 5, wherein  $R^1$  is cyclobutyl or cyclopentyl, wherein  $R^1$  substituted with  $-NR^7C(=O)R^8$  or  $(C_6-C_{14})aryl$ . New Claim 44 is dependent on Claim 5 which, as discussed above, is allowable over the cited art. In addition, the cited art does not disclose or suggest that  $R^1$  is cyclobutyl or cyclopentyl, wherein  $R^1$  substituted with  $-NR^7C(=O)R^8$  or  $(C_6-C_{14})aryl$ . For at least this additional reason, new Claim 44 is allowable over the cited art.

In view of the foregoing, examination and allowance of all pending claims in the application is respectfully requested.

Please charge any appropriate fee to cover this submission to Pfizer Deposit Account No. 16-1445. A duplicate copy of this sheet is enclosed.

Respectfully submitted,



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